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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,518	08/24/2001	Mark J. Jaroszeski	93004	2429
9355	7590	03/24/2004	EXAMINER	
ALLEN, DYER, DOPPELT, MILBRATH & GILCHRIST, PA P.O. BOX 3791 ORLANDO, FL 32802-3791			ANGELL, JON E	
			ART UNIT	PAPER NUMBER
			1635	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

*SPM*

### Office Action Summary

Application No.	JAROSZESKI ET AL.	
09/939,518		
Examiner	Art Unit	
J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 23 December 2003.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,2,4,6,8,10-12,14,16,18 and 20-52 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) 21-36 is/are allowed.

6) Claim(s) 1,2,4,6,8,10-12,14,16,18,20 and 37-52 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_.

**DETAILED ACTION**

1. This Action is in response to the communication filed on 12/23/03. The amendment has been entered. New claims 37-52 have been added. Claims 1, 2, 4, 6, 8, 10-12, 14, 16, 18 and 20-52 are currently pending in the application and are examined herein.
2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 2, 4, 6, 8, 10-12, 14, 16, 18 and 20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hofmann et al. (U.S. Patent 6,055,453, published April 25, 2000), for the reasons of record, summarized below.

Hofmann teaches a method for facilitating a delivery of a desired molecule, here nucleic acids, antisense nucleic acids, Ribozymes, polypeptides, and polynucleotides (such as expression vectors) encoding metabolic enzymes and proteins (see col. 12, lines 14 and 34; col. 13, lines 13, 24 and 31-31), into a target tissue comprising a cell; and applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the

cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example see col. 1, lines 6-13; col. 10, lines 3-56; and col. 11, lines 63-65);

Wherein the low-level electric field has a field strength comprising 10V/cm-20kV/cm and for a duration of 10 $\mu$ s-**100ms** (Emphasis added; see col. 10, lines 3-41);

Wherein the electric field comprises multiple square pulse waveforms (see col.10, line 55-56);

Wherein the introducing step comprises needle injection (i.e. syringe) (see col. 13, lines 31-45 and);

Wherein the target tissue is skin, tumor, muscle, ovary, prostate, lung, heart, kidney, colon, testis, melanoma, etc. (see col. 14, lines 10-30).

And wherein the method further comprises a means for constructing a plasmid comprising a DNA and cDNA encoding a molecule of interest (see col. 12, line 61-col. 13, line 11).

Hofmann also teaches a system comprising a means for facilitating the delivery of a desired molecule, here nucleic acids, antisense nucleic acids, Ribozymes, polypeptides, and polynucleotides (such as expression vectors) encoding metabolic enzymes and proteins (see col. 12, lines 14 and 34; col. 13, lines 13, 24 and 31-31), into a target tissue comprising a cell; and a means for applying a substantial continuous low-level electric field to the target tissue for a duration sufficient to effect a change in porosity of the cell of the target tissue sufficient to facilitate entry of a desired molecule into an interior of a cell (for example see col. 1, lines 6-13; col. 10, lines 3-56; and col. 11, lines 63-65);

Wherein the low-level electric field has a field strength comprising 10V/cm-20kV/cm and for a duration of 10 $\mu$ s-**100ms** (Emphasis added; see col. 10, lines 3-41);

Wherein the electric field comprises multiple square pulse waveforms (see col.10, line 55-56);

Wherein the means for introducing the molecule comprises needle injection (i.e. syringe) (see col. 13, lines 31-45 and);

Wherein the target tissue is skin, tumor, muscle, ovary, prostate, lung, heart, kidney, colon, testis, melanoma, etc. (see col. 14, lines 10-30);

And wherein the system comprises a means for constructing a plasmid comprising a DNA and cDNA encoding a molecule of interest (see col. 12, line 61-col. 13, line 11).

#### *Response to Arguments*

5. Applicant's arguments filed 12/23/03 have been fully considered but they are not persuasive.

Applicants' argue that the claims have been further limited to include the step of effecting a change in porosity of the cell of the target tissue in response to the application of the electric field sufficient to facilitate entry of a desired molecule into an interior of the cell (see p. 12). Furthermore, Applicants' acknowledge that the instant claims are not limited to a method consisting of only the recited steps and no other steps (i.e. a single pulse). Applicants contend that Hofmann does not teach effecting a change in porosity in response to the application of the electric field wherein the electric field is a single continuous low-level electric field applied for 100ms-20mins.

In response, it is acknowledged that Hofmann does not explicitly teach that an application of a single continuous low-level electric field applied for 100ms results in a change in porosity of the target cell such that it allows the entry of the desired molecule into the cell. However, since Hofmann does teach a method comprising the application of a single continuous low-level electric field which meets all of the parameters set forth in the instant claims, then the effect of any single continuous electric field taught by Hofmann must, by necessity, have the same effect on the cell as the claimed application of the single continuous electric field. That is, since Hofmann teaches a method that includes the application of a single continuous low-level electric field that is within the parameters of the claimed method, then the effect of applying a single pulse of Hofmann must have the same effect as applying a single pulse of the claimed method. As such, a single pulse of the method taught by Hofmann would necessarily result in a change in porosity of the target cell such that it would allow the entry of the desired molecule into the cell. Therefore, Applicants arguments are not persuasive and the rejection is not withdrawn.

It is noted, that amending the independent claims (1 and 11) to narrow the scope of the claims to a method consisting of a single pulse, as indicated; or, alternatively, amending the independent claims to be drawn to a method for facilitating the delivery of a desired molecule into a target tissue wherein said method “consists essentially of” the steps indicated (i.e. change “comprising” of line 2 of claims 1 and 11 to “consisting essentially of”) would obviate this rejection.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

Art Unit: 1635

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. New claims 37-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. Claims 37 and 45 are independent claims drawn to methods for facilitating the delivery of a desired molecule into a target tissue comprising administering a continuous low-level electric field to the target tissue for a duration of 110ms to 20 minutes.

9. However, the specification does not appear to explicitly indicate that the method can comprise a continuous low-level electric field applied to the target tissue for a duration of 110ms. It is acknowledged that the specification teaches that the method can comprise the application of a single electric field for a duration in the range of 100ms to 20 minutes. In order to claim a method comprising the administration of an electric field for 110ms the specification must have explicit support for this limitation. Scanning the specification, it is acknowledged that the specification has support for administering an electric field for 100ms and 200ms, but it does not appear that specification has explicit support for 110ms. Should Applicants disagree, Applicants are asked to identify, by page and line number, where the specification discloses application of an electric field for 110ms.

Art Unit: 1635

10. Claims 38-44 and 46-52 are dependent claims that must encompass all of the limitations of the independent claims (37 and 45). Therefore claims 38-44 and 46-52 are also rejected for the same reasons.

***Response to Arguments***

11. Applicant's arguments filed 12/23/03 have been fully considered but they are not persuasive.

12. Applicants argue that Hofmann does not teach applying an electric field for 110ms.

13. In response, it is acknowledged that Hofmann does not teach the instant limitation.

However, as indicated above, the instant specification does not appear to have explicit support for 110ms. Therefore, this limitation is considered new matter and the rejection set forth is appropriate.

***Miscellaneous***

The objection to claim 30 has been withdrawn in view of amendment.

***Allowable Subject Matter***

14. Claims 21-29, 31-36 are allowed because the claims are limited to a system and method comprising applying an electric field having a duration of 200ms to 20 mins.

***Conclusion***

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1635

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.  
Art Unit 1635



DAVE T. NGUYEN  
PRIMARY EXAMINER